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September 15, 1992

Document Processing Center (TS-790)
Office of Pollution Prevention and Toxics
U. S. Environmental Protection Agency
401 M Street, SW
Washington, DC 20460
Attn: 8(e) Coordinator (CAP Agreement)

Dear Sir or Madam:

Subject: Report submitted in accordance with guidelines established by the U. S. Environmental Protection Agency Registration and Agreement for the TSCA 8(e) Compliance Audit Program

Report submitted by: Eastman Kodak Company
343 State Street
Rochester, NY 14650
(716) 724-4000
CAP Agreement Identification Number (8ECAP-0039)

This report pertains to (4-cyanophenyl)carbamic acid, phenyl ester (synonym: phenyl N-(p-cyanophenyl)carbamate) [CAS# 71130-54-6] and is being submitted because of effects observed during a subacute feeding study in rats. The title of the report being submitted is: "Basic Toxicity of Phenyl N-(p-cyanophenyl)carbamate". This report is being identified as a study involving other than human effects (Unit II.B.2.b of CAP Agreement).

Groups of five male rats were fed diets containing 0.1% or 1.0% of the test material for twelve days. Animals at the high-dose level either died or were euthanatized in poor condition by study Day 7; the mean methemoglobin concentration was 33% at necropsy. Dose-related abnormalities observed included reduced feed consumption and body weight gain, decreased absolute and relative liver and kidney weights, increased absolute and relative spleen weights, and hematologic changes. At the high-dose level, three serum enzymes and urea nitrogen were increased. Gross and histopathologic changes observed in the high-dose group included brown discolored lungs, congestion of the spleen, liver, and kidneys, and hematologic changes. No treatment-related effects were observed in the low-dose group.

The test material has been used internally. It is not sold as a pure chemical or in a mixture.

RECEIVED 9/16/95

Questions regarding this submission should be addressed to:

Mr. William Hart
Eastman Kodak Company
Corporate Health and Environment Laboratories
Rochester, NY 14652-3615
(716) 722-5991

Sincerely,

R. Hays Bell

R. Hays Bell, Ph.D.
Vice President
Corporate Health, Safety and Environment
(716) 722-5036

RHB:DRG
Enclosure

114395E
TX-79-36

Basic Toxicity of Phenyl N-(p-cyanophenyl)carbamate

Toxicology Section

Written by: J. R. Harr

March 6, 1979

114395E
TX-79-36

Basic Toxicity of Phenyl N-(p-cyanophenyl)carbamate,

The single dose oral LD50 in male rats and mice is greater than 3200 mg/kg. Signs of toxicity are weakness and dark colored eyes characteristic of methemoglobinemia. Cutaneous effects after 24 hours under an occlusive dressing were slight irritation. The compound produced weak to moderate sensitization in three of five guinea pigs. Ten daily doses produced slight additive effects (erythema) in three of five guinea pigs, and slightly reduced effects (erythema) in one of the other two pigs. There was no evidence of percutaneous absorption. Crystals of compound placed in the conjunctival sac produced transient irritation. The irritation was moderate in 2/3 washed eyes and slight in the other eyes.

Three groups of five male rats were fed powdered feed with 2% corn oil and 1.0, 0.1 or 0.0% compound for 12 days. Dosage rates were 220, 82 and 0.0 mg/kg/day. The 1.0% dose group lost 20% of their body weight in four days, became moribund and were necropsied on the 7th day of dosage. At necropsy, the mean concentration of methemoglobin in this group was 33%. The other two treatment groups (0.1% and control) were necropsied after 12 days of dosage. Effects were compound and strongly dose related. They included a slight to great decrease in body weight, weight gain, feed consumption, relative liver weight (to body weight) and direct liver and kidney weight; increases in the relative (to body weight) weight of the kidney (slight) and spleen (moderate), the

direct weight of the spleen (moderate) and the concentration of GOT, GPT, LDH and urea nitrogen (slight to great) in sera from the 1.0% group and destruction of neutrophils and erythrocytes with appearance of their early and immature forms in peripheral blood. Gross lesions were brownish colored lungs and congestion of the spleen, liver and kidney. Microscopic lesions were congestion of the spleen.

The dose and rate of production of methemoglobin was determined in five groups of three male rats given 200, 20 or 2 mg/kg of the compound per os, or a negative or positive control (30 mg/kg of m-dinitrobenzene). Two and four hours after dosage the concentration of methemoglobin in the three principal groups was respectively 52 and 39% (two and four hours, 200 mg/kg), 28 and 10% (20 mg/kg), and 2.2 and 0.9% (2 mg/kg). Comparable concentrations in the negative and positive control groups were respectively 1.5 and 0.7% and 52 and 43%. The test compound forms methemoglobin approximately 1/6 as rapidly as m-dinitrobenzene. Toxicity effects erythrocytes, neutrophils, the liver and the sites of hematopoiesis and granulocytopoiesis.

The no-effect concentration in the standard germination test for lettuce was 10 mg/l. Concentration of 100 mg/l effected hypocotyl and root growth of lettuce. The no-effect concentration in the germination test of ryegrass and radish, and for early plant growth of marigold, radish, corn and lettuce was greater than 100 mg/l. The static 96 hour LC50 for fathead minnows, daphnids, snails and flatworms was also greater than 100 mg/l. The Kodak Park Industrial Laboratory reported that the compound was insoluble in water and had a chemical oxygen demand of 1.85 g O_2/g of sample.

JRH:bdo

Summary of Basic Toxicity

Chemical Phenyl N-(p-cyanophenyl)carbamate

Date 3-6-79

LD_{50} (mg/kg) P.O. Rats >3200 Mice >3200

Remarks: Weakness, dark colored eyes (methemoglobin)

Skin Irritation (covered) Slight Moderate Strong Absorption: Not evident

Remarks:

Eye Irritation

	Slight	Moderate	Strong	Fluorescein stain Cornea	Fluorescein stain Adnexa
No. washed	1/3	2/3			
No. unwashed	3/3				

Remarks:

Skin Sensitization Potential No. guinea pigs 5

None 2/5 Weak 2/5 Moderate 1/5 Potent 0/5

Remarks:

Repeated (10 days) Skin Application (uncovered) No. guinea pigs 5

Remarks: Additive effects in 3/5 guinea pigs.
Reduced effects in 1/5 guinea pigs.

Other Tests

Summary of Basic Toxicity--2

Repeated Feeding No. rats/group 5 No. days 12 Carrier 2% corn oil

	1.0 %	0.1 %
Weight gain	↓3	↓1
Feed intake	↓3	↓1
Signs/behavior	poor condition	N

Clinical Chemistry:

GOT	↑3	N
GPT	↑3	N
LDH	↑2	N
AP	N	N
UN	↑1	N
Gluc.	N	N

Hematology	1.0 %	0.1 %
Hgb.	↓1	N
Hct.	N	N
WBC	N	N
Diff.	↑3	↑2

Organ Weight:

Liver		
Abs.	↓3	↓1
Rel.	↓3	↓1
Kidney		
Abs.	↓2	↓1
Rel.	↑1	N
Spleen		
Abs.	↑2	↑2
Rel.	↑2	↑2

Pathology 1.0% group-killed after 7 days; methemoglobin 33%. Eyes dark, loss of condition. Gross lesions were brown tinged lungs, congestion of spleen, liver, kidney. Microscopic changes were congestion of the spleen, and destruction and regeneratio of neutrophils and erythrocytes.

Repeated Inhalation ND Concn._____ No. rats_____ No. days_____

Wt. change_____ Signs/behavior_____

Hemat.: Hgb._____ Hct._____ WBC_____ Diff._____

Clinc. Chem.: GOT_____ GPT_____ LDH_____ AP_____ UN_____ Gluc._____

Pathology

Static 96 hour LC_{50} mg/l XXXX

Fathead minnows >100 Daphnids >100 Snails >100 Flatworms >100

No effect concn. mg/l XXXX

	Germination	Hypocotyl Growth	Root Growth
Ryegrass	>100	>100	>100
Radish	>100	>100	>100
Lettuce	>100	10	10

Remarks:

Summary of Basic Toxicity--3

No effect concn. mg/l ~~XXX~~ Early Plant Growth

Marigold	>100
Radish	>100
Corn	>100
Lettuce	>100

Remarks:

Industrial Laboratory (g O_2/g sample)

BOD_5 ND BOD_{20} ND TOD ND COD 1.85*

*Insoluble in water

Historical Control Data (5/77)

	Mean	SD	Extremes
GPT	70	16	29-135
GOT	174	32	114-304
LDH	1410	494	459-3135
AP	669	170	341-1166
UN	19.0	2.9	9.0-29.0
Glucose	141	17.6	94-216
Hgb	14.6	1.1	10.5-18.7
Hct	45.8	3.4	35-58
WBC	13,955	4330	6700-46,500
Poly	18.4	7.4	4-50
Band	2.1	2.1	0-11
Lymph	78.1	8.5	44-95

Legend

↑	Increased
↓	Decreased
1	Slight
2	Moderate
3	Great
N	Normal
ND	Not done

Addendum to Basic Toxicity Report 114395E, TX-79-36

Phenyl N-(p-Cyanophenyl)Carbamate

An earlier repeated feeding study done on this compound failed to establish a no-effect dose for spleen and red blood cell changes. Therefore, an additional repeated study was done to establish this level.

Three groups of five male rats each were fed concentrations of 0.1 and 0.01% of phenyl n-(p-cyanophenyl)carbamate in the diet with 1.0% corn oil for 10 consecutive days. These concentrations provide daily doses of 87 and 9 mg/kg. Feed consumption was slightly reduced in both treated groups and the 0.1% animals had a slightly reduced body weight gain. The skin of the tails and ears and the eyes of the high dose rats were pale.

The absolute and relative weights of liver, kidneys and spleens of the low dosed animals (0.01%) and the liver and kidney weights of the high dosed (0.1%) rats were comparable to the control. Spleen weights (absolute/relative) of the 0.1% animals were moderately increased.

Hemoglobin and the mean corpuscular hemoglobin concentrations were slightly decreased, the mean corpuscular volume was increased and the red blood cell morphology was abnormal in the high dosed rats. These parameters were not affected by the 0.01% treatment.

Neither treatment affected the serum levels of glutamic oxaloacetic and glutamic pyruvic transaminases, lactic dehydrogenase,

alkaline phosphatase, urea nitrogen and glucose. Compound related pathology noted at necropsy was large, dark congested spleens (5/5) in the high dosed animals.

Histologically, compound related changes included splenic congestion and hemosiderosis and increased prominence of hepatic extramedullary hematopoiesis. These changes may have been due to the red blood cell destruction seen in this group of animals. The low dose treatment produced no compound related gross or histologic pathology.

The data collected from this additional repeated feeding study establishes a no-effect dose between 0.01 and 0.1% (9-87 mg/kg/day) for phenyl n-(p-cyanophenyl)carbamate.

WK:mlt
5/29/80

SUMMARY OF BASIC TOXICITY-- Phenyl n-(p-cyanophenyl)carbamate

Repeated Exposure **Feeding** Drinking Water Gavage Inhalation

No. rats/group 5 No. exposures 10 No. days 11 Carrier Corn oil 1.0%

Units of exposure: % mg/kg mg/m^3 ppm

Exposure concentration:	0.1	0.01		0.1	0.01
Weight gain	+1	N	Hematology:		
Feed intake	+1	+1	Hgb.	+1	N
			Hct.	+1	N
Daily dose (mg/kg/day)	87	9.0	WBC	N	N
			Diff.	N	N
Signs/behavior	Ab*	N	RBC	+1**	N
			MCV	+1	N
*Paleness of tail, feet, eyes & ears.			MCH	N	N
**Red cell morphology = micro & macrocytosis, anisocytosis, polychromasia			MCHC	+1	N

Clinical chemistry:			Organ weight:		
GOT	N	N	Liver		
GPT	N	N	Abs.	N	N
LDH	N	N	Rel.	N	N
AP	N	N	Kidney		
UN	N	N	Abs.	N	N
Glucose	N	N	Rel.	N	N
			Spleen		
			Abs.	+2	N
			Rel.	+2	N

Gross pathology: 0.1% - Enlarged dark spleens
0.01% - None

Histopathology: 0.1% - Splenic congestion, hemosiderosis, hepatic extra medullary hematopoesis.
0.01% - None

Site of toxic action: 0.1% - Spleen and red blood cells
0.01% - None

Legend

+	Increased
-	Decreased
1	Slight
2	Moderate
3	Great
N	Normal
ND	Not done

4/79:bdo

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

R. Hays Bell, Ph.D.
Vice President, Corporate Health, Safety, and Environment
Eastman Kodak Company
343 State Street
Rochester, New York 14650

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

APR 18 1995

EPA acknowledges the receipt of information submitted by your organization under Section 8(e) of the Toxic Substances Control Act (TSCA). For your reference, copies of the first page(s) of your submission(s) are enclosed and display the TSCA §8(e) Document Control Number (e.g., 8EHQ-00-0000) assigned by EPA to your submission(s). Please cite the assigned 8(e) number when submitting follow-up or supplemental information and refer to the reverse side of this page for "EPA Information Requests".

All TSCA 8(e) submissions are placed in the public files unless confidentiality is claimed according to the procedures outlined in Part X of EPA's TSCA §8(e) policy statement (43 FR 11110, March 16, 1978). Confidential submissions received pursuant to the TSCA §8(e) Compliance Audit Program (CAP) should already contain information supporting confidentiality claims. This information is required and should be submitted if not done so previously. To substantiate claims, submit responses to the questions in the enclosure "Support Information for Confidentiality Claims". This same enclosure is used to support confidentiality claims for non-CAP submissions.

Please address any further correspondence with the Agency related to this TSCA 8(e) submission to:

Document Processing Center (7407)
Attn: TSCA Section 8(e) Coordinator
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
Washington, D.C. 20460-0001

EPA looks forward to continued cooperation with your organization in its ongoing efforts to evaluate and manage potential risks posed by chemicals to health and the environment.

Sincerely,

Terry R. O'Bryan

Terry R. O'Bryan
Risk Analysis Branch

Enclosure 12495A

Triage of 8(e) Submissions

Date sent to triage: APR 20 [illegible]

NON-CAP (CAP)

Submission number: 12495A

TSCA Inventory: (Y) N D

Study type (circle appropriate):

Group 1 - Dick Clements (1 copy total)

(ECO) (AQUATO)

Group 2 - Ernie Falke (1 copy total)

(ATOX) (SBTOX) (SEN) w/NEUR

Group 3 - Elizabeth Margosches (1 copy each)

STOX	CTOX	EPI	RTOX	GTOX
STOX/ONCO	CTOX/ONCO	IMMUNO	CYTO	NEUR

Other (FATE, EXPO, MET, etc.): _____

Notes:

THIS IS THE ORIGINAL 8(e) SUBMISSION; PLEASE REFILE AFTER TRIAGE DATABASE ENTRY

For Contractor Use Only

entire document: (NO) 2 **pages** 1,2 **pages** 1,2,[illegible]

Notes:

Contractor reviewer : TDR **Date:** 5/29/95

CECATS\TRIAGE TRACKING DBASE ENTRY FORM

CECATS DATA:
Submission # 8EHQ- 0992 - 12495 SEQ. A

TYPE: (INT.) SUPP FLWP

SUBMITTER NAME: E. I. Dupont de Nemours and Company

SUB. DATE: 09/15/92 OTS DATE: 09/24/92 CSRAD DATE: 02/16/95

CHEMICAL NAME:

#
71130-54-6

INFORMATION REQUESTED: FLWP DATE:
0501 NO INFO REQUESTED
0502 INFO REQUESTED (TECH)
0503 INFO REQUESTED (VOL ACTIONS)
0504 INFO REQUESTED (REPORTING RATIONALE)

DISPOSITION:
(0639) REFER TO CHEMICAL SCREENING
(0678) CAP NOTICE

VOLUNTARY ACTIONS:
(0401) NO ACTION REPORTED
0402 STUDIES PLANNED/UNDERWAY
0403 NOTIFICATION OF WORKERS/OTHERS
0404 LABEL/MSDS CHANGES
0405 PROCESS/HANDLING CHANGES
0406 APP./USE DISCONTINUED
0407 PRODUCTION DISCONTINUED
0408 CONFIDENTIAL

INFORMATION TYPE:		P F C
0201	ONCO (HUMAN)	01 02 04
0202	ONCO (ANIMAL)	01 02 04
0203	CELL TRANS (IN VITRO)	01 02 04
0204	MUTA (IN VITRO)	01 02 04
0205	MUTA (IN VIVO)	01 02 04
0206	REPRO/TERATO (HUMAN)	01 02 04
0207	REPRO/TERATO (ANIMAL)	01 02 04
0208	NEURO (HUMAN)	01 02 04
0209	NEURO (ANIMAL)	01 02 04
0210	ACUTE TOX. (HUMAN)	01 02 04
0211	CHR. TOX. (HUMAN)	01 02 04
0212	ACUTE TOX. (ANIMAL)	01 02 04
(0213)	SUB ACUTE TOX (ANIMAL)	01 (02) 04
0214	SUB CHRONIC TOX (ANIMAL)	01 02 04
0215	CHRONIC TOX (ANIMAL)	01 02 04

INFORMATION TYPE:		P F C
0216	EPI/CLIN	01 02 04
0217	HUMAN EXPOS (PROD CONTAM)	01 02 04
0218	HUMAN EXPOS (ACCIDENTAL)	01 02 04
0219	HUMAN EXPOS (MONITORING)	01 02 04
0220	ECO/AQUA TOX	01 02 04
0221	ENV. OCCC/REL/FATE	01 02 04
0222	EMER INCI OF ENV CONTAM	01 02 04
0223	RESPONSE REQEST DELAY	01 02 04
0224	PROD/COMP/CHEM ID	01 02 04
0225	REPORTING RATIONALE	01 02 04
0226	CONFIDENTIAL	01 02 04
0227	ALLERG (HUMAN)	01 02 04
0228	ALLERG (ANIMAL)	01 02 04
0239	METAB/PHARMACO (ANIMAL)	01 02 04
0240	METAB/PHARMACO (HUMAN)	01 02 04

INFORMATION TYPE:		P F C
0241	IMMUNO (ANIMAL)	01 02 04
0242	IMMUNO (HUMAN)	01 02 04
0243	CHEM/PHYS PROP	01 02 04
0244	CLASTO (IN VITRO)	01 02 04
0245	CLASTO (ANIMAL)	01 02 04
0246	CLASTO (HUMAN)	01 02 04
0247	DNA DAM/REPAIR	01 02 04
0248	PROD/USE/PROC	01 02 04
0251	MSDS	01 02 04
0299	OTHER	01 02 04

Atox/Sbtox/Sen

TRIAGE DATA: NON-CBI INVENTORY
(YES)
CAS SR NO
(NO TERMINI)

ONGOING REVIEW
YES (DROP/REFER)
NO (CONTINUE)
REFER

SPECIES
RAT
mus
GP
Fish

TOXICOLOGICAL CONCERN:
~~LOW~~
(MED)
HIGH

USE:

PRODUCTION:

COMMENTS

8(E)-12495A

L/L/M/L/L/M/~~M~~ L

ACUTE ORAL TOXICITY OF RATS IS OF LOW CONCERN BASED ON AN LD50 GREATER THAN 3200 MG/KG. SIGNS OF TOXICITY WERE WEAKNESS AND DARK COLORED EYES CHARACTERISTIC OF METHEMOGLOBINEMIA. INCIDENCES OF MORTALITY WERE NOT GIVEN.

ACUTE ORAL TOXICITY OF MICE IS OF LOW CONCERN BASED ON AN LD50 GREATER THAN 3200 MG/KG. SIGNS OF TOXICITY WERE WEAKNESS AND DARK COLORED EYES CHARACTERISTIC OF METHEMOGLOBINEMIA. INCIDENCES OF MORTALITY WERE NOT GIVEN.

SUBACUTE ORAL TOXICITY IN MALE RATS IS OF MEDIUM CONCERN BASED ON METHEMOGLOBINEMIA. DOSAGES (DIET, INTENDED TO BE 12-DAYS, 5/GROUP) WERE 0.1% (80 MG/KG/DAY AS DETERMINED BY THE STUDY AUTHORS) AND 1% (220 MG/KG/DAY AS DETERMINED BY THE STUDY AUTHORS). AT 80 MG/KG/DAY, THERE WERE NO CLINICAL OR HISTOPATHOLOGICAL EFFECTS. AT 220 MG/KG/DAY, CLINICAL SIGNS INCLUDED A DECREASE IN FOOD CONSUMPTION AND A 20% DECREASE IN BODY WEIGHTS SUCH THAT ANIMALS BECAME MORIBUND AND WERE SACRIFICED ON THE 7TH DAY OF DOSING. OTHER TREATMENT-RELATED EFFECTS AT 220 MG/KG/DAY INCLUDED MODERATELY TO GREATLY INCREASED SERUM GOT, GPT, AND LDH; SLIGHTLY INCREASED BLOOD UREA NITROGEN; GREATLY DECREASED RELATIVE LIVER WEIGHT; INCREASED RELATIVE KIDNEY (SLIGHT) AND SPLEEN (MODERATE) WEIGHT; GROSSLY-OBSERVED BROWN-TINGED LUNGS AND CONGESTION OF SPLEEN, LIVER, AND KIDNEY; DESTRUCTION OF NEUTROPHILS AND ERYTHROCYTES WITH APPEARANCE OF THEIR EARLY AND IMMATURE FORMS IN PERIPHERAL BLOOD; A MEAN METHEMOGLOBIN LEVEL OF 33 PERCENT. TREATMENT-RELATED EFFECTS AT 80 MG/KG/DAY INCLUDED MODERATELY INCREASED RELATIVE SPLEEN WEIGHT, SLIGHTLY DECREASED RELATIVE LIVER WEIGHT, AND SLIGHTLY DECREASED FOOD INTAKE AND WEIGHT GAIN. IN A COMPANION GAVAGE STUDY ON METHEMOGLOBIN PRODUCTION IN GROUPS OF 3 MALE RATS, METHEMOGLOBIN LEVELS WERE 1.5% AT 2 HOURS AND 0.7% AT 4 HOURS AT 0 MG/KG, 2.2 AND 0.9% AT 2 MG/KG, 28 AND 10% AT 20 MG/KG, AND 52 AND 39% AT 200 MG/KG. THE TEST COMPOUND CAUSED METHEMOGLOBIN TO FORM ABOUT 1/6 AS RAPIDLY AS THE POSITIVE CONTROL M-DINITROBENZENE.

DERMAL IRRITATION IN GUINEA PIGS IS OF LOW CONCERN BASED ON SLIGHT IRRITATION (3/5) FROM AN OCCLUDED EXPOSURE TO TEST SUBSTANCE. DOSAGE AMOUNT AND DURATION WERE NOT REPORTED.

EYE IRRITATION IN RABBITS IS OF LOW CONCERN BASED ON SLIGHT (1/3, WASHED, 3/3, UNWASHED) TO MODERATE (2/3, WASHED) IRRITATION FROM EXPOSURE TO TEST SUBSTANCE. DOSAGE AMOUNT AND DURATION WERE NOT REPORTED.

DERMAL SENSITIZATION IN GUINEA PIGS IS OF MEDIUM CONCERN BASED ON MILD (2/5) AND MODERATE (1/5) SENSITIZATION RESPONSES FROM A 10-DAY UNOCCLUDED EXPOSURE TO TEST SUBSTANCE. DOSAGE AMOUNT, DURATION, AND SENSITIZATION TEST PROTOCOL WERE NOT REPORTED.

SUBACUTE ORAL TOXICITY IN MALE RATS IS OF ~~MEDIUM~~ CONCERN. DOSAGES

Low

(DIET, 10-DAYS, 5/GROUP) WERE 0.1% (87 MG/KG/DAY AS DETERMINED BY THE STUDY AUTHORS) AND 0.01% (9 MG/KG/DAY AS DETERMINED BY THE STUDY AUTHORS). CLINICAL SIGNS INCLUDED SLIGHTLY REDUCED FEED CONSUMPTION IN BOTH GROUPS. AT 87 MG/KG/DAY, RATS HAD SLIGHTLY REDUCED BODY WEIGHT GAIN, THE SKIN OF THE TAILS AND EARS WAS PALE, AND THE EYES WERE PALE. THE ABSOLUTE AND RELATIVE WEIGHTS OF LIVER, KIDNEY, AND SPLEEN OF THE 9 MG/KG/DAY, AND THE LIVER AND KIDNEY WEIGHTS OF THE 87 MG/KG/DAY GROUP WERE COMPARABLE TO CONTROLS. SPLEEN WEIGHTS OF THE 87 MG/KG/DAY GROUP WERE MODERATELY INCREASED AND AT NECROPSY WERE LARGE, DARK, AND CONGESTED (5/5). IN THE 87 MG/KG/DAY GROUP, HEMOGLOBIN AND THE MEAN CORPUSCULAR HEMOGLOBIN CONCENTRATIONS WERE SLIGHTLY DECREASED, THE MEAN CORPUSCULAR VOLUME WAS INCREASED, AND THE RED BLOOD CELL MORPHOLOGY WAS ABNORMAL. HISTOLOGICAL EFFECTS INCLUDED SPLENIC CONGESTION AND HEMOSIDEROSIS AND INCREASED PROMINENCE OF HEPATIC EXTRAMEDULLARY HEMATOPOIESIS.

"12495A"="ACUTE ORAL TOXICITY IN RATS IS OF LOW CONCERN BASED ON AN LD50 GREATER THAN 3200 MG/KG. SIGNS OF TOXICITY WERE WEAKNESS AND DARK COLORED EYES CHARACTERISTIC OF METHEMOGLOBINEMIA. INCIDENCES OF MORTALITY WERE NOT GIVEN. ACUTE ORAL TOXICITY IN MICE IS OF LOW CONCERN BASED ON AN LD50 GREATER THAN 3200 MG/KG. SIGNS OF TOXICITY WERE WEAKNESS AND DARK COLORED EYES CHARACTERISTIC OF METHEMOGLOBINEMIA. INCIDENCES OF MORTALITY WERE NOT GIVEN. SUBACUTE ORAL TOXICITY IN MALE RATS IS OF MEDIUM CONCERN BASED ONMETHEMOGLOBINEMIA. DOSAGES (DIET, INTENDED TO BE 12 DAYS, 5/GROUP) WERE 0.1% (80 MG/KG/DAY AS DETERMINED BY THE STUDY AUTHORS) AND 1% (220 MG/KG/DAY AS DETERMINED BY THE STUDY AUTHORS). AT 80 MG/KG/DAY, THERE WERE NO CLINICAL OR HISTOPATHOLOGICAL EFFECTS. AT 220 MG/KG/DAY, CLINICAL SIGNS INCLUDED A DECREASE IN FOOD CUNSUMPTION AND A 20% DECREASE IN BODY WEIGHTS SUCH THAT ANIMALS BECAME MORIBUND AND WERE SACRIFICED ON THE 7TH DAY OF DOSING. OTHER TREATMENT-RELATED EFFECTS AT 220 MG/KG/DAY INCLUDED MODERATELY TO GREATLY INCREASED SERUM GOT, GPT, AND LDH; SLIGHTLY INCREASED BLOOD UREA NITROGEN; GREATLY DECREASED RELATIVE LIVER WEIGHT; INCREASED RELATIVE KIDNEY (SLIGHT) AND SPLEEN (MODERATE) WEIGHT; GROSSLY-OBSERVED BROWN-TINGED LUNGS AND CONGESTION OF SPLEEN, LIVER, AND KIDNEY; DESTRUCTION OF NEUTROPHILS AND ERYTHROCYTES WITH APPEARANCE OF THEIR EARLY AND IMMATURE FORMS IN PERIPHERAL BLOOD; A MEAN METHEMOGLOBIN LEVEL OF 33 PERCENT. TREATMENT-RELATED EFFECTS AT 80 MG/KG/DAY INCLUDED MODERATELY INCREASED RELATIVE SPLEEN WEIGHT, SLIGHTLY DECREASE RELATIVE LIVER WEIGHT, AND SLIGHTLY DECREASED FOOD INTAKE AND WEIGHT GAIN. IN A COMPANION GAVAGE STUDY ON METHEMOGLOBIN PRODUCTION IN GROUPS OF 3 MALE RATS, METHEMOGLOBIN LEVELS WERE 1.5% AT 2 HOURS AND 0.7% AT 4 HOURS AT 0 MG/KG, 2.2 AND 0.9% AT 2 MG/KG, 28 AND 10% AT 20 MG/KG, AND 52 AND 39% AT 200 MG/KG. THE TEST COMPOUND CAUSED METHEMOGLOBIN TO FORM ABOUT 1/6 AS RAPIDLY AS THE POSITIVE CONTROL M-DINITROBENZENE. DERMAL IRRITATION IN GUINEA PIGS IS OF LOW CONCERN BASED ON SLIGHT IRRITATION (3/5) FROM AN OCCLUDED EXPOSURE TO TEST SUBSTANCE. DOSAGE AMOUNT AND DURATION WERE NOT REPORTED. EYE IRRITATION IN RABBITS IS OF LOW CONCERN BASED ON SLIGHT (1/3 WASHED, 3/3 UNWASHED) TO MODERATE (2/3 WASHED) IRRITATION FROM EXPOSURE TO TEST SUBSTANCE. DOSAGE AMOUNT AND DURATION WERE NOT REPORTED. DERMAL SENSITIZATION IN GUINEA PIGS IS OF MEDIUM CONCERN BASED ON MILD (2/5) AND MODERATE (1/5) SENSITIZATION RESPONSES FROM A 10 DAY UNOCCLUDED EXPOSURE TO TEST SUBSTANCE. DOSAGE AMOUNT, DURATION, AND SENSITIZATION TEST PROTOCOL WERE NOT REPORTED. SUBACUTE ORAL TOXICITY IN MALE RATS IS OF LOW CONCERN. DOSAGES (DIET, 10 DAYS, 5/GROUP) WERE 0.1% (87 MG/KG/DAY AS DETERMINED BY THE STUDY AUTHORS) AND 0.01% (9 MG/KG/DAY AS DETERMINED BY THE STUDY AUTHORS). CLINICAL SIGNS INCLUDED SLIGHTLY REDUCED FEED CUNSUMPTION IN BOTH GROUPS.

AT 87 MG/KG/DAY, RATS HAD SLIGHTLY REDUCED BODY WEIGHT GAIN, THE SKIN OF THE TAILS AND EARS WAS PALE, AND THE EYES WERE PALE. THE ABSOLUTE AND RELATIVE WEIGHTS OF LIVER, KIDNEY, AND SPLEEN OF THE 9 MG/KG/DAY, AND THE LIVER AND KIDNEY WEIGHTS OF THE 87 MG/KG/DAY GROUP WERE COMPARABLE TO CONTROLS. SPLEEN WEIGHTS OF THE 87 MG/KG/DAY GROUP WERE MODERATELY INCREASED AND AT NECROPSY WERE LARGE, DARK, AND CONGESTED (5/5). IN THE 87 MG/KG/DAY GROUP, HEMOGLOBIN AND THE MEAN CORPUSCULAR HEMOGLOBIN CONCENTRATIONS WERE SLIGHTLY DECREASED, THE MEAN CORPUSCULAR VOLUME WAS INCREASED, AND THE RED BLOOD CELL MORPHOLOGY WAS ABNORMAL. HISTOLOGICAL EFFECTS INCLUDED SPLENIC CONGESTION AND HEMOSIDEROSIS AND INCREASED PROMINENCE OF HEPATIC EXTRAMEDULLATY HEMATOPOIESIS. WEIGHTS OF

AQUATIC TOXICITY TO THE FATHEAD MINNOW, P. PROMELAS IS OF LOW CONCERN WITH A 96 HOUR LC50 > 100 MG/L.

AQUATIC TOXICITY TO DAPHNIA IS OF LOW CONCERN WITH A 96 HOUR LC50 > 100 MG/L.

TOXICITY TO THE RYEGRASS, LOLIUM PERENNE, IS OF LOW CONCERN WITH A NOEC > 100 MG/L BASED ON GERMINATION.

TOXICITY TO THE RYEGRASS, LOLIUM PERENNE, IS OF LOW CONCERN WITH A NOEC > 100 MG/L BASED ON HYPOCOTYL GROWTH.

TOXICITY TO THE RYEGRASS, LOLIUM PERENNE, IS OF LOW CONCERN WITH A NOEC > 100 MG/L BASED ON ROOT GROWTH.

TOXICITY TO THE RADISH, RAPHANUS SATIVA, IS OF LOW CONCERN WITH A NOEC > 100 MG/L BASED ON GERMINATION.

TOXICITY TO THE RADISH, RAPHANUS SATIVA, IS OF LOW CONCERN WITH A NOEC > 100 MG/L BASED ON HYPOCOTYL GROWTH.

TOXICITY TO THE RADISH, RAPHANUS SATIVA, IS OF LOW CONCERN WITH A NOEC > 100 MG/L BASED ON ROOT GROWTH.

TOXICITY TO THE RADISH, RAPHANUS SATIVA, IS OF LOW CONCERN WITH A NOEC > 100 MG/L BASED ON EARLY PLANT GROWTH.

TOXICITY TO THE LETTUCE, LACTUCA SATIVA, IS OF LOW CONCERN WITH A NOEC > 100 MG/L BASED ON GERMINATION.

TOXICITY TO THE LETTUCE, LACTUCA SATIVA, IS OF LOW CONCERN WITH A NOEC > 10 MG/L BASED ON HYPOCOTYL GROWTH.

TOXICITY TO THE LETTUCE, LACTUCA SATIVA, IS OF LOW CONCERN WITH A NOEC > 10 MG/L BASED ON ROOT GROWTH.

TOXICITY TO THE LETTUCE, LACTUCA SATIVA, IS OF LOW CONCERN WITH A NOEC > 100 MG/L BASED ON EARLY PLANT GROWTH.

TOXICITY TO MARIGOLD IS OF LOW CONCERN WITH A NOEC > 100 MG/L BASED ON EARLY PLANT GROWTH.

TOXICITY TO THE CORN, ZEA MAYS, IS OF LOW CONCERN WITH A NOEC > 100 MG/L BASED ON EARLY PLANT GROWTH.

THIS TEST SUBSTANCE IS INSOLUBLE.

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